Obesity Management Strategies: Endoscopic Bariatric Therapy

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Disclosure

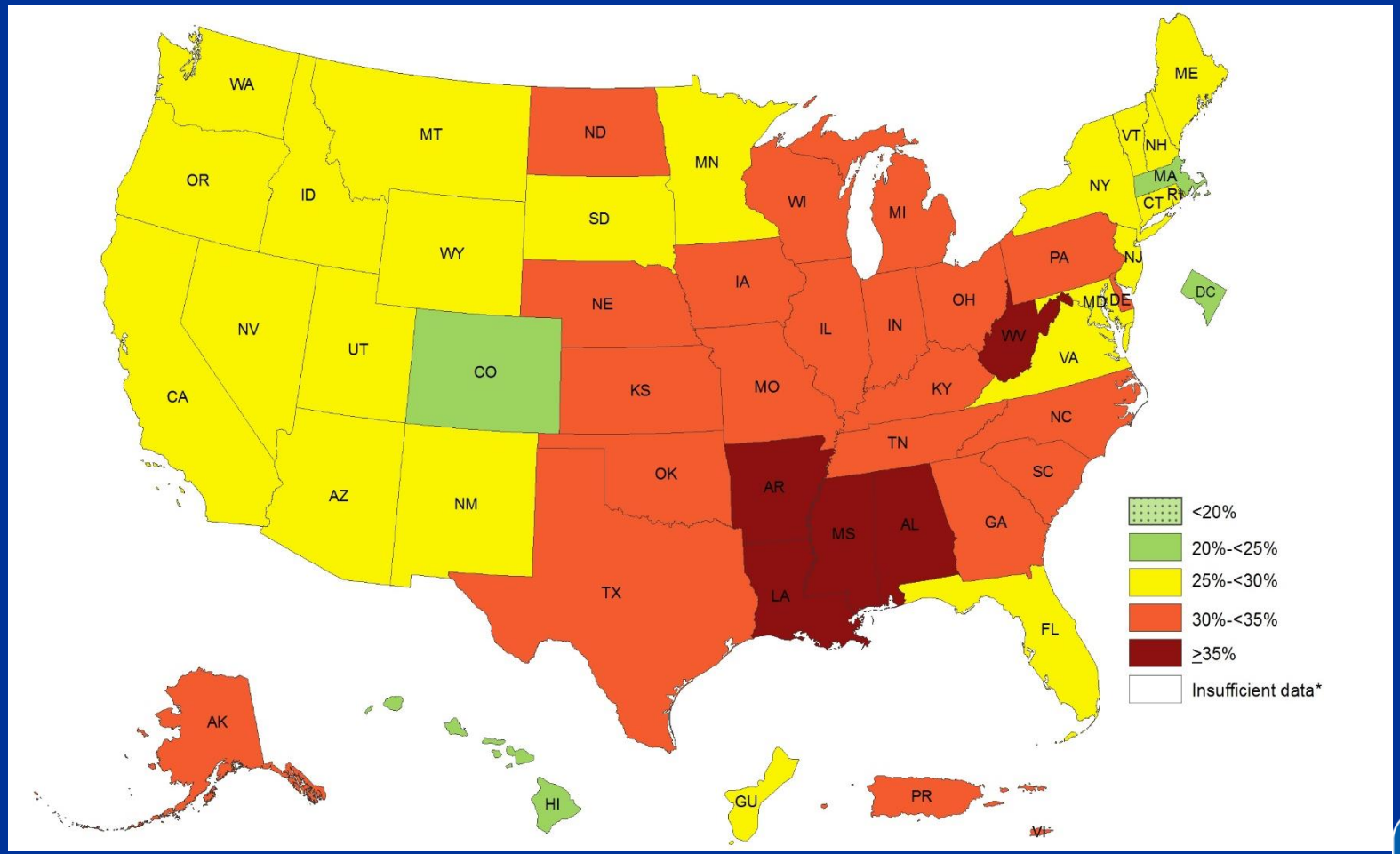
- The following are my disclosures. Potential conflicts of interest have been resolved.

  - No disclosures

Obesity in America

- 36.5% of US population has obesity
- Higher prevalence among African American (48.1%) and Hispanic (42.5%) populations, and people with lower income
- Multiple associated comorbidities include heart disease, stroke, diabetes, certain cancers
- Estimated annual cost $147 billion (average healthcare costs $1400/year higher for patients with obesity vs. those without)

Prevalence of Self-Reported Obesity Among U.S. Adults by State and Territory, BRFSS, 2016



*Sample size <50 or the relative standard error (dividing the standard error by the prevalence) ≥ 30%.

Obesity management

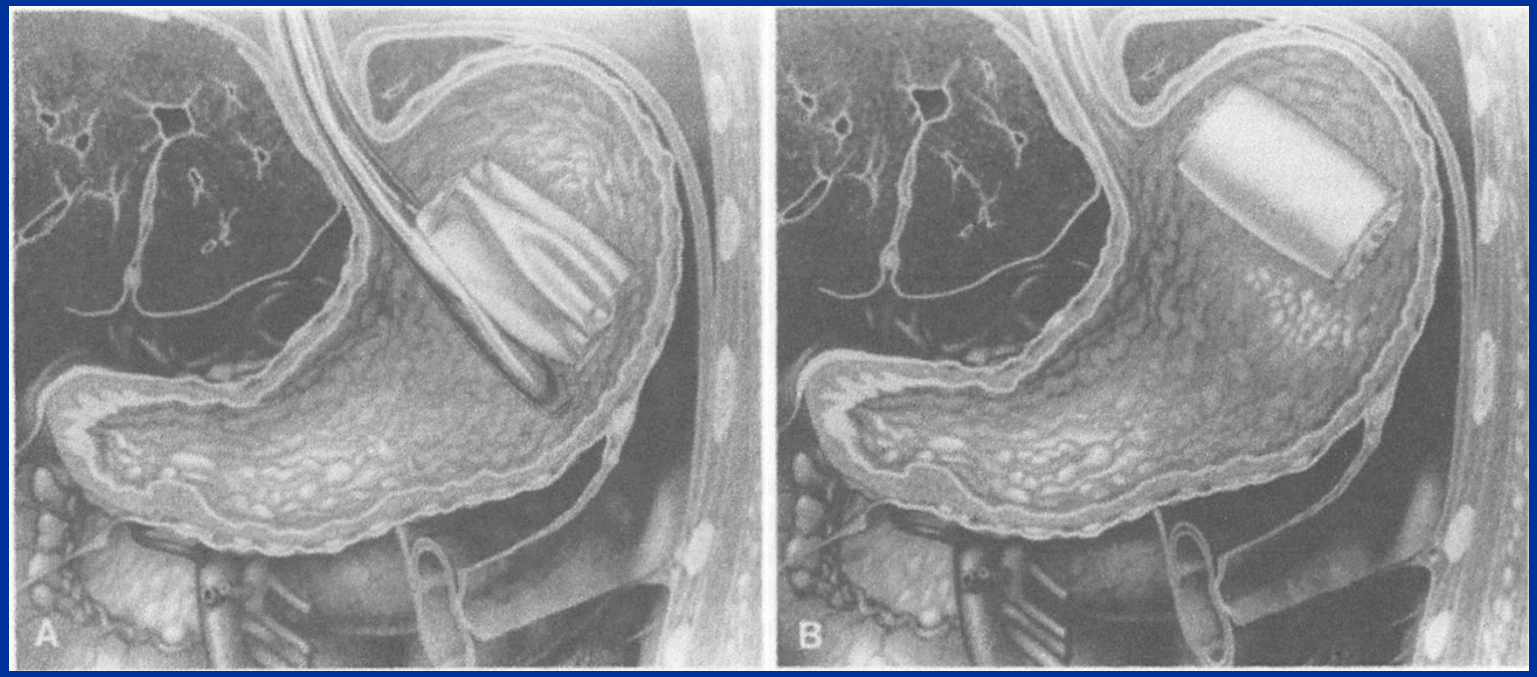
- Lifestyle modification
- Medications
- Surgery
- Endoscopy

Primary endoscopic therapy

- American Society for Gastrointestinal Endoscopy (ASGE) position statement supports use of endoscopic bariatric therapy (EBT) in conjunction with a multidisciplinary weight loss program
- Consider EBT in patients who:
  - Have failed weight loss or maintenance with lifestyle intervention alone
  - Meet BMI criteria for particular treatment modalities
  - Have medical conditions that require weight loss of additional therapy (e.g. bridge therapy to weight loss surgery)
- Current approved and investigational devices include space-occupying devices, tissue apposition devices, and nutrient-diverting devices

Sullivan S, Kumar N, Edmundowicz SA, et al. ASGE position statement on endoscopic bariatric therapies in clinical practice. *Gastrointest Endosc.* 2015;82(5):767-772.

Garren-Edwards Gastric Bubble



VelchikMG, KramerM, Stunkard AJ, AlaviA. Effect of the Garren-Edwards Gastric Bubble on gastric emptying. JNuclMed.1989;30:692–6.

Garren-Edwards Gastric Bubble

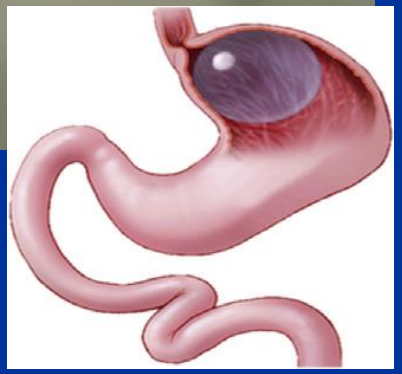
- First described in 1982 and FDA approved in 1985
- Air filled balloon, placed endoscopically
- Pulled from market in 1992 due to adverse events including gastric mucosa injury, small bowel obstruction following deflation and migration, poor efficacy
- Likely reasons for failure:
  - Material: polyurethane, deflated too easily
  - Shape: cylindrical, with edges leading to ulcers
  - Size: 220 mL volume, 400 mL minimum to decrease food intake
- After this experience no intragastric balloon was approved by the FDA until 2015

Gaur S, Levy S, Mathus-Vliegen L, Chuttani R. Balancing risk and reward: a critical review of the intragastric balloon for weight loss. *Gastrointestinal endoscopy* 2015; 81(6):1330-36.

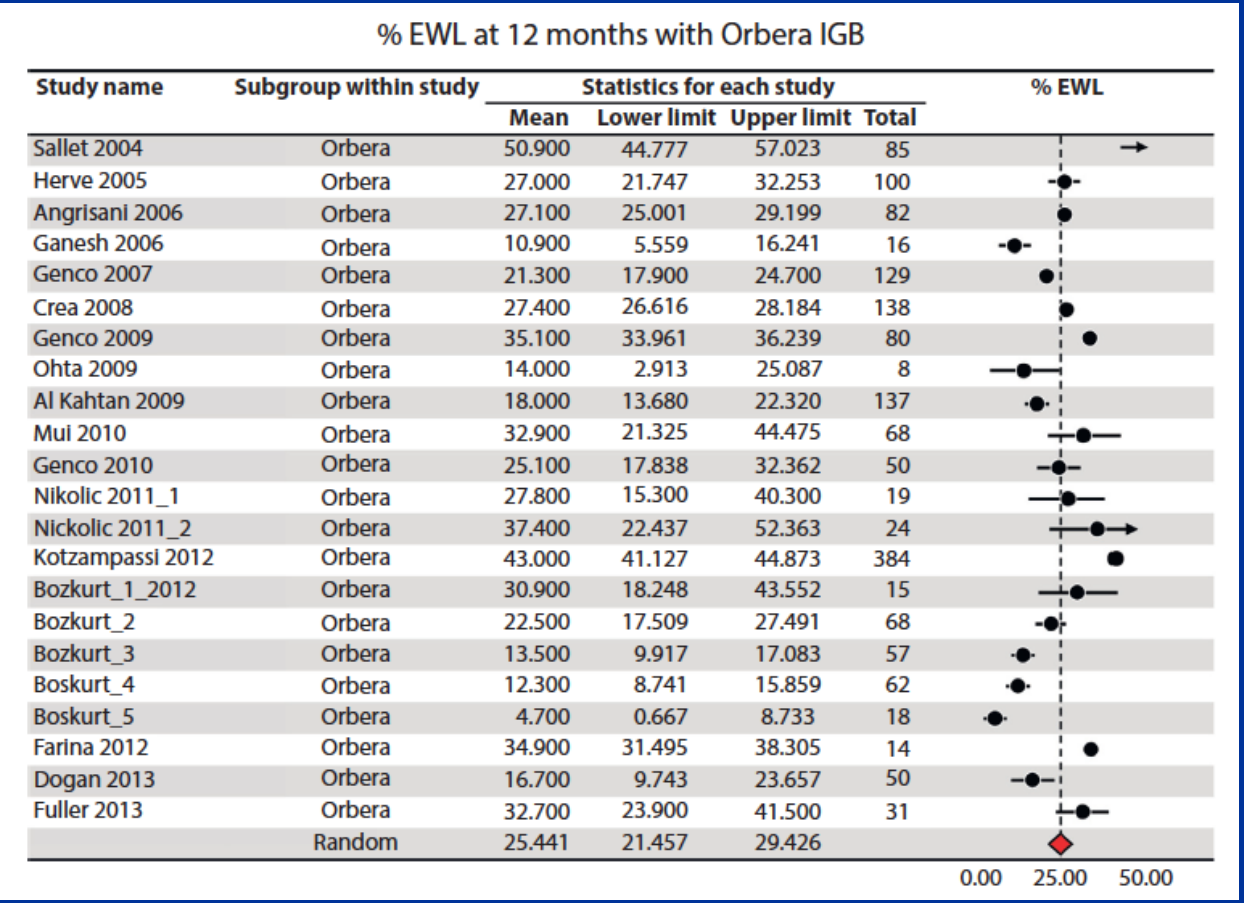
Fluid-filled single balloon: Orbera

- Spherical silicone balloon
- Placed endoscopically, filled with saline (often containing methylene blue)
- Filled to 400-700 mL
- Remains in place for 6 months, removed endoscopically
- Introduced 1991, previously called Bioenteric Intragastric Balloon (BIB)
- Has been evaluated in multiple studies, available elsewhere since 1990s

Allergan, Irvine, CA



Orbera efficacy

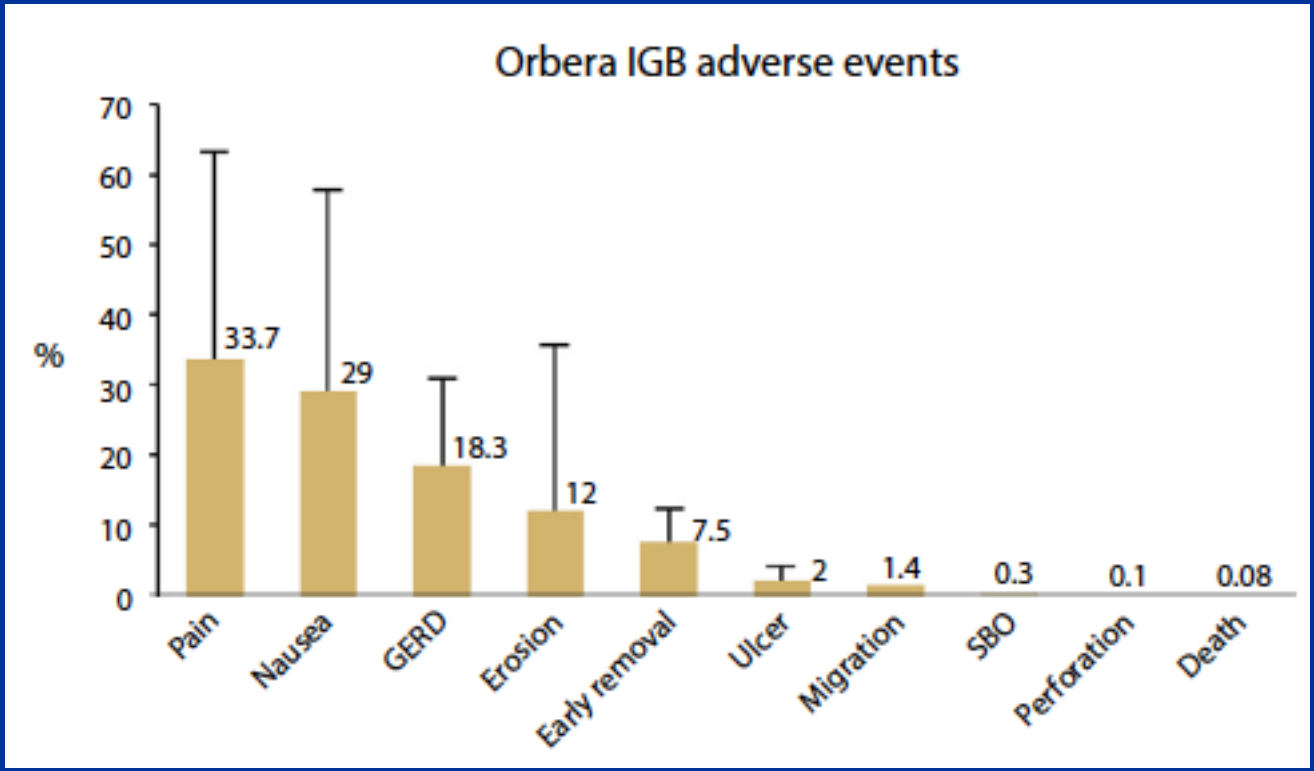


% EWL at 12 months with Orbera IGB

Study name	Subgroup within study	Statistics for each study				% EWL
		Mean	Lower limit	Upper limit	Total	
Sallet 2004	Orbera	50.900	44.777	57.023	85	
Herve 2005	Orbera	27.000	21.747	32.253	100	
Angrisani 2006	Orbera	27.100	25.001	29.199	82	
Ganesh 2006	Orbera	10.900	5.559	16.241	16	
Genco 2007	Orbera	21.300	17.900	24.700	129	
Crea 2008	Orbera	27.400	26.616	28.184	138	
Genco 2009	Orbera	35.100	33.961	36.239	80	
Ohta 2009	Orbera	14.000	2.913	25.087	8	
Al Kahtan 2009	Orbera	18.000	13.680	22.320	137	
Mui 2010	Orbera	32.900	21.325	44.475	68	
Genco 2010	Orbera	25.100	17.838	32.362	50	
Nikolic 2011_1	Orbera	27.800	15.300	40.300	19	
Nickolic 2011_2	Orbera	37.400	22.437	52.363	24	
Kotzampassi 2012	Orbera	43.000	41.127	44.873	384	
Bozkurt_1_2012	Orbera	30.900	18.248	43.552	15	
Bozkurt_2	Orbera	22.500	17.509	27.491	68	
Bozkurt_3	Orbera	13.500	9.917	17.083	57	
Boskurt_4	Orbera	12.300	8.741	15.859	62	
Boskurt_5	Orbera	4.700	0.667	8.733	18	
Farina 2012	Orbera	34.900	31.495	38.305	14	
Dogan 2013	Orbera	16.700	9.743	23.657	50	
Fuller 2013	Orbera	32.700	23.900	41.500	31	
	Random	25.441	21.457	29.426		

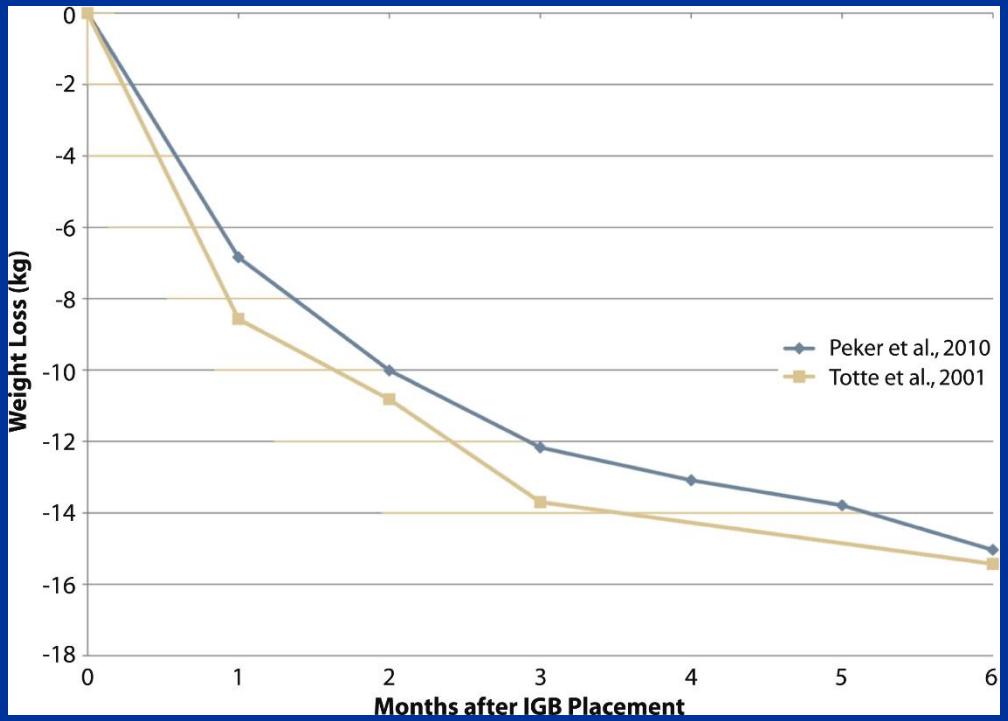
Abu Dayyeh BK, et al. ASGE Bariatric Endoscopy Task Force systematic review and meta-analysis assessing the ASGE PIVI thresholds for adopting endoscopic bariatric therapies. *Gastrointestinal endoscopy.* 2015;82(3):425-438 e425.

Orbera adverse events



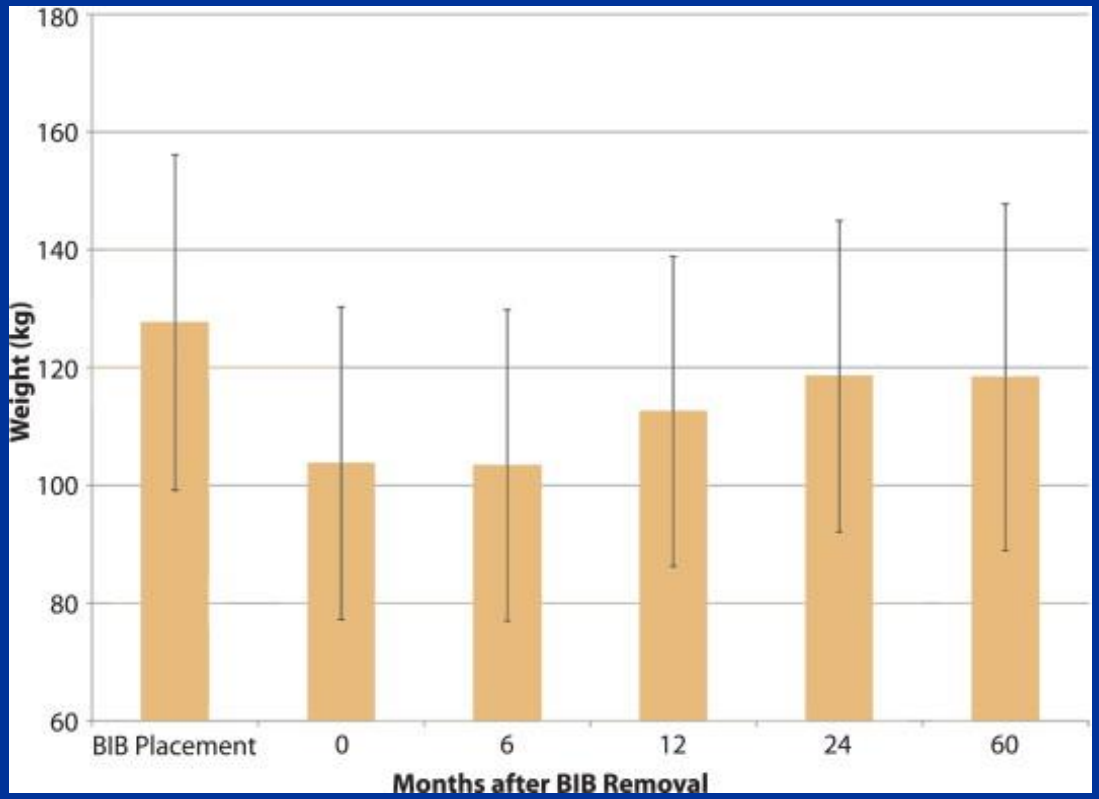
Abu Dayyeh BK, et al. ASGE Bariatric Endoscopy Task Force systematic review and meta-analysis assessing the ASGE PIVI thresholds for adopting endoscopic bariatric therapies. *Gastrointestinal endoscopy.* 2015;82(3):425-438 e425.

Orbera: weight loss kinetics



Gaur S, Levy S, Mathus-Vliegen L, Chuttani R. Balancing risk and reward: a critical review of the intragastric balloon for weight loss. *Gastrointestinal endoscopy* 2015; 81(6):1330-36.

Orbera: durability of weight loss



Gaur S, Levy S, Mathus-Vliegen L, Chuttani R. Balancing risk and reward: a critical review of the intragastric balloon for weight loss. *Gastrointestinal endoscopy* 2015; 81(6):1330-36.

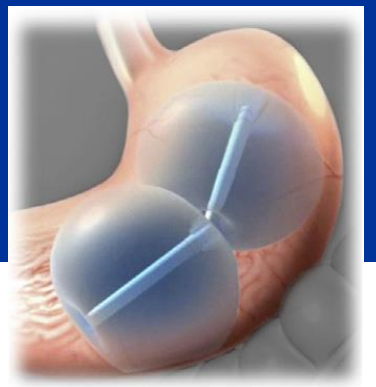
Contraindications (FDA)

- Prior GI or bariatric surgery
- Inflammatory disease of GI tract e.g. esophagitis, ulcer disease, cancer, Crohn's
- Potential upper GI bleeding conditions e.g. varices, telangectasias; or congenital anomalies e.g. atresias
- Large hiatal hernia > 5 cm or smaller with severe reflux symptoms
- Structural abnormality in esophagus or pharynx e.g. stricture or diverticulum
- Achalasia or other severe motility disorder
- Gastric mass
- Coagulopathy
- Cirrhosis or other serious comorbid condition
- Serious or uncontrolled psychiatric illness
- Alcohol or drug addiction
- Unwillingness to take PPI, stop NSAIDs, or participate in diet and behavior program
- Pregnancy or breast feeding

Fluid-filled dual balloon: ReShape

- Two silicone balloons connected by flexible shaft
- Placed endoscopically, each filled 375 or 450 mL saline + methylene blue
- Designed to prevent migration
- Removed endoscopically at 6 months

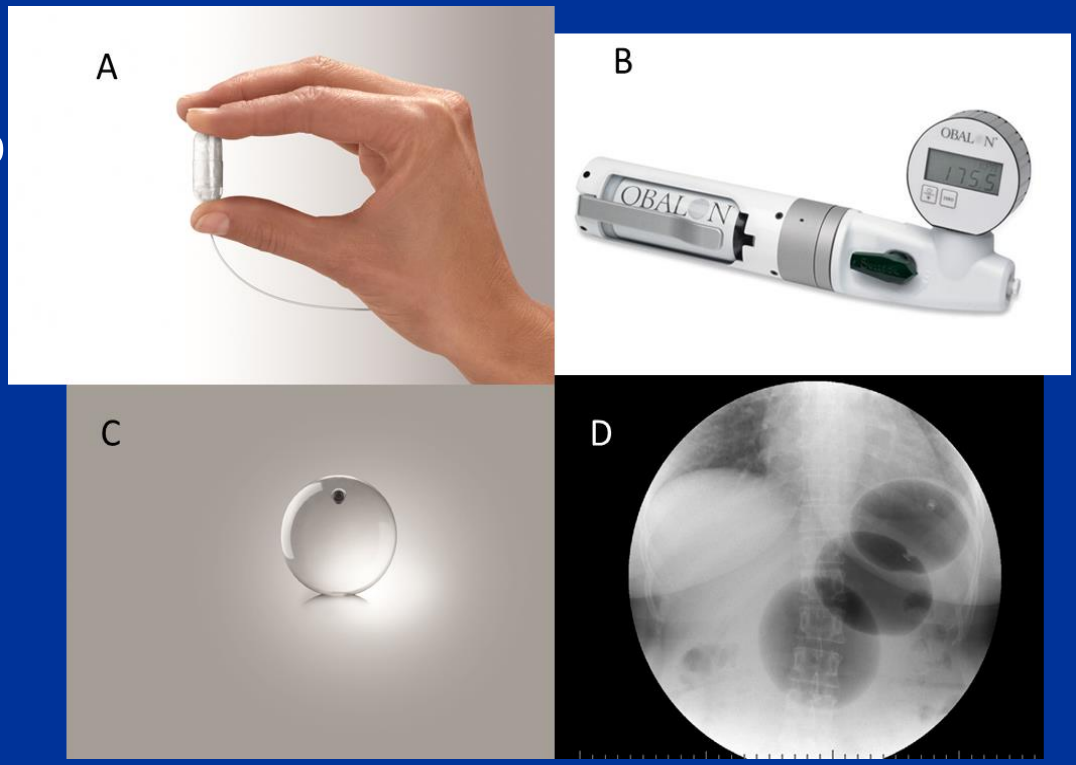
- FDA approved 2015
- Product has recently been discontinued



ReShape Medical, San Clemente, CA

Gas-filled swallowed balloon: Obalon

- Gelatin capsule with attached catheter, swallowed under fluoro
- Inflate with 250 mL nitrogen-mix gas
- Can swallow up to 3 balloons over 6 month course
- Removed endoscopically
- Per FDA, average weight loss 14.4 lbs or 6.6% total weight



A. Swallowable capsule containing balloon
B. Inflation device
C. Gas-filled balloon
D. Radiograph of three deployed balloons in vivo
Obalon Therapeutics, Carlsbad, CA.

FDA Summary of safety and effectiveness data (SSED): Obalon Balloon system.
https://www.accessdata.fda.gov/cdrh_docs/pdf16/P160001b.pdf

Comparison of US pivotal trial data

Table 2. Intragastric Balloon US Pivotal Trial Study Design, Number of Subjects, Weight Loss, Responder Rate, and SAE Rate in all Patients in the Intention-to-Treat Analysis

Device	Study design	No. of subjects		BMI (kg/m^2)		Percent TBWL, all subjects		Active group responder rate (% of subjects or ≥5% TBWL or ≥25% EWL)	SAE rate
		Control group	Active group	Control group	Active group	Control group	Active group		
Orbera Intragastric Balloon[12]	Randomized, open label, BMI 30–40, 12-visit lifestyle intervention, weight loss outcome at 6 mo	130	125	35.4 ± 2.7	35.2 ± 3.2	3.3 ± 5.0%	10.2 ± 6.6%	79.2%	10%
Reshape Integrated Dual Balloon System[20]	Randomized, sham controlled, BMI 30–40, 6-visit lifestyle intervention, weight loss outcome at 6 mo	139	187	35.4 ± 2.6	35.3 ± 2.8	3.3%	6.8%	48.8%	10.6%
Obalon Balloon System[13]	Randomized, sham controlled, BMI 30–40, 7-visit lifestyle intervention, all balloons removed 6 mo after first balloon, weight loss outcome at 6 mo	189	198	35.4 ± 2.7	35.1 ± 2.7	3.4 ± 5.0%	6.6 ± 5.1%	62.1%	0.5%

BMI, body mass index; EWL, excess weight loss; SAE; serious adverse event; TBWL, total body weight loss.

Serious adverse events included:
- hospital admissions for nausea, vomiting, pain, or device removal (75%)
- 1 esophageal mucosal tear, 1 contained esophageal perforation, 1 bleeding gastric ulcer, 1 aspiration pneumonitis (ReShape)
- 1 gastric outlet obstruction, 1 gastric perforation, 1 aspiration pneumonia, 2 esophageal tears, 1 laryngospasm, 1 infected balloon (Orbera)
- 1 bleeding gastric ulcer (Obalon)

Sullivan S, Edmundowicz SA, Thompson CC. Endoscopic bariatric and metabolic therapies: new and emerging technologies. Gastroenterology 2017; 152:1791-1801.

Adverse event comparison

Table 3. Common Non-SAE in Intragastric Balloon US Pivotal Trials

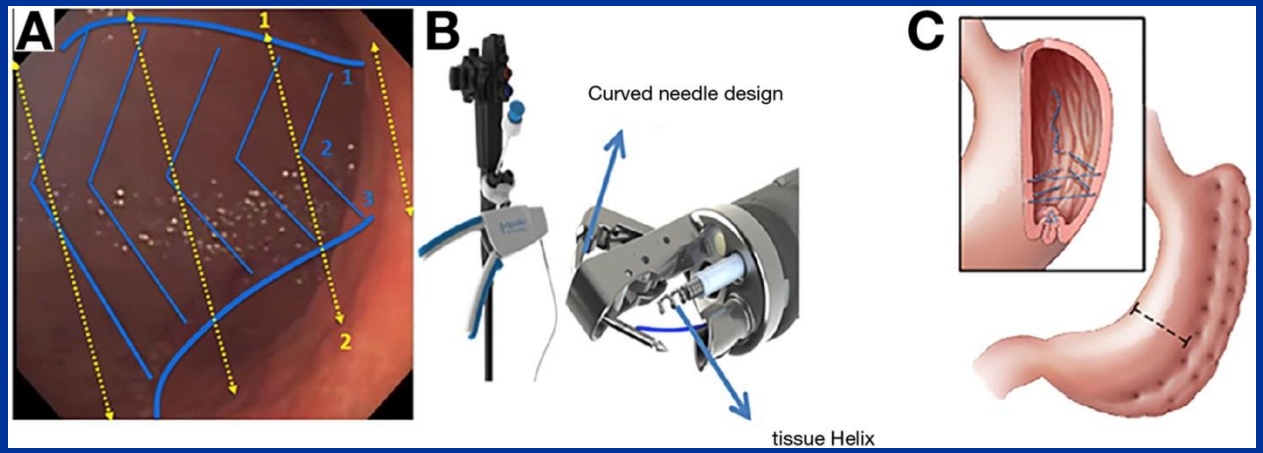
Adverse event	ReShape (%)	Orbera (%)	Obalon (%)
Vomiting	86.7	86.8	17.3
Nausea	61.0	75.6	56.0
Abdominal pain	54.5	57.5	72.6
Gastric ulcer	35.2[a]	0	0.9
Dyspepsia	17.8	21.3	16.9[c]
Eructation	16.7	24.4	9.2
Abdominal discomfort	13.3	6.3	0
Abdominal distension	11.0	17.5	14.6
Erosive gastritis	9.1	0.6	7.1[b]
GERD	6.8	30.0	(see dyspepsia)
Erosive esophagitis	0.4	0.6	1.8
Constipation	5.3	0	2.7
Diarrhea	3.0	13.1	8.3

GERD, gastroesophageal reflux disease; SAE, serious adverse event.
[a]After design modification of the distal tip of the ReShape Balloon, the ulcer rate decreased to 10%.
[b]Composite of erythema, erosion, inflammation, or polyp.
[c]Composite of dyspepsia and GERD.

Sullivan S, Edmundowicz SA, Thompson CC. Endoscopic bariatric and metabolic therapies: new and emerging technologies. Gastroenterology 2017; 152:1791-1801.

Endoscopic sleeve gastroplasty (ESG)

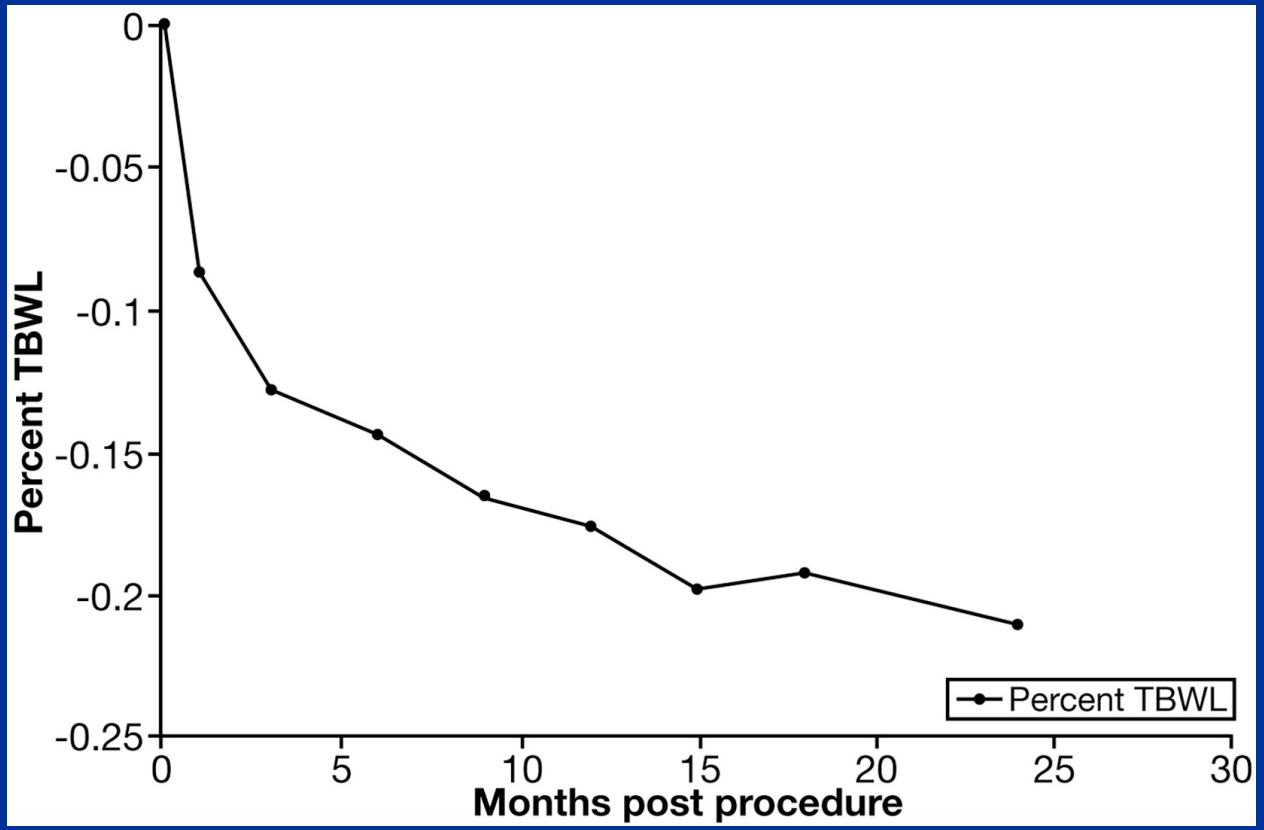
- Endoscopic suturing device used to create a gastric sleeve
- Uses FDA approved device. 98 min average procedure time.
- Fits on end of double channel endoscope.
- Curved needle driver produces full-thickness sutures



A. Suturing pattern used
B. Endoscopic suturing device (Apollo Overstitch)
C. Depiction of procedure

Abu Dayyeh BK, Acosta A, Camilleri M, et al. Endoscopic sleeve gastroplasty alters gastric physiology and induces loss of body weight in obese individuals. Clin Gastroenterol Hepatol 2015; epub ahead of print

ESG Weight loss kinetics



Sharaiha RZ, Kumta NA, Saumoy M et al. Endoscopic sleeve gastroplasty significantly reduces body mass index and metabolic complications in obese patients. Clinical Gastroenterology and Hepatology 2017; 15: 504-510.

ESG effect on obesity-related comorbidities

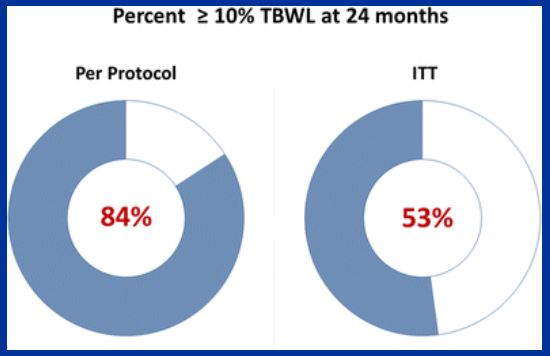
Table 2. Post-ESG Improvement in Weight and Medical Comorbidities at 12 Months (N = 53)

	Before ESG, mean (SD)	12 months after ESG, mean (SD)	*P* value
HgbA1c, % (all patients)	6.1 (1.1)	5.5 (0.48)	.05
HgbA1c, % (only diabetes and prediabetes)	6.6 (1.2)	5.6 (0.51)	.02
Waist circumference, *cm*	119.66 (14.05)	92.75 (5.85)	<.001
SBP, *mm Hg*	129.02 (13.44)	122.23 (11.69)	.023
LDL, *mg/dL*	121.62 (38.61)	124.27 (27.82)	.786
TG, *mg/dL*	131.84 (83.19)	92.36 (39.43)	.017
ALT, *mg/dL*	32.28 (16.43)	20.68 (11.44)	<.001

Sharaiha RZ, Kumta NA, Saumoy M et al. Endoscopic sleeve gastroplasty significantly reduces body mass index and metabolic complications in obese patients. Clinical Gastroenterology and Hepatology 2017; 15: 504-510.

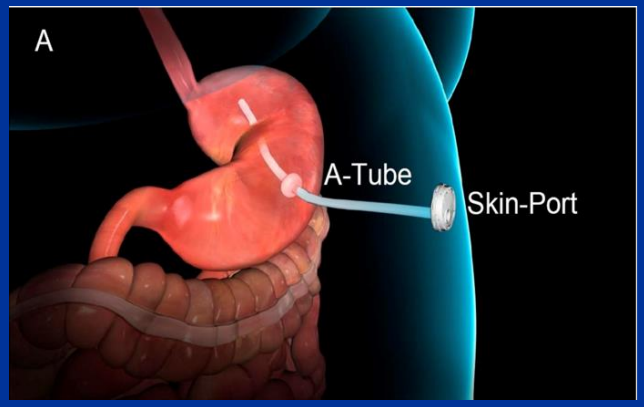
ESG multicenter study

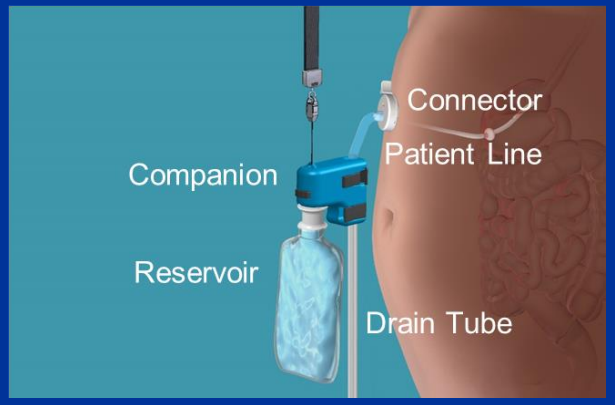
- 3 center study in US and Spain
- 248 patients
- 15.7% TWL at 6 months, 18.6% at 24 months
- Five serious adverse events: inflammatory fluid collections (adjacent to fundus), self-limited hemorrhage, pulmonary embolism, pneumothorax; none required surgery



Lopez-Nava G, Sharaiha RZ, Vargas EJ et al. Endoscopic sleeve gastroplasty for obesity: a multicenter study of 248 patients with 24 months follow-up. Obesity Surgery 2017; 27(10): 2649-55.

Aspiration therapy



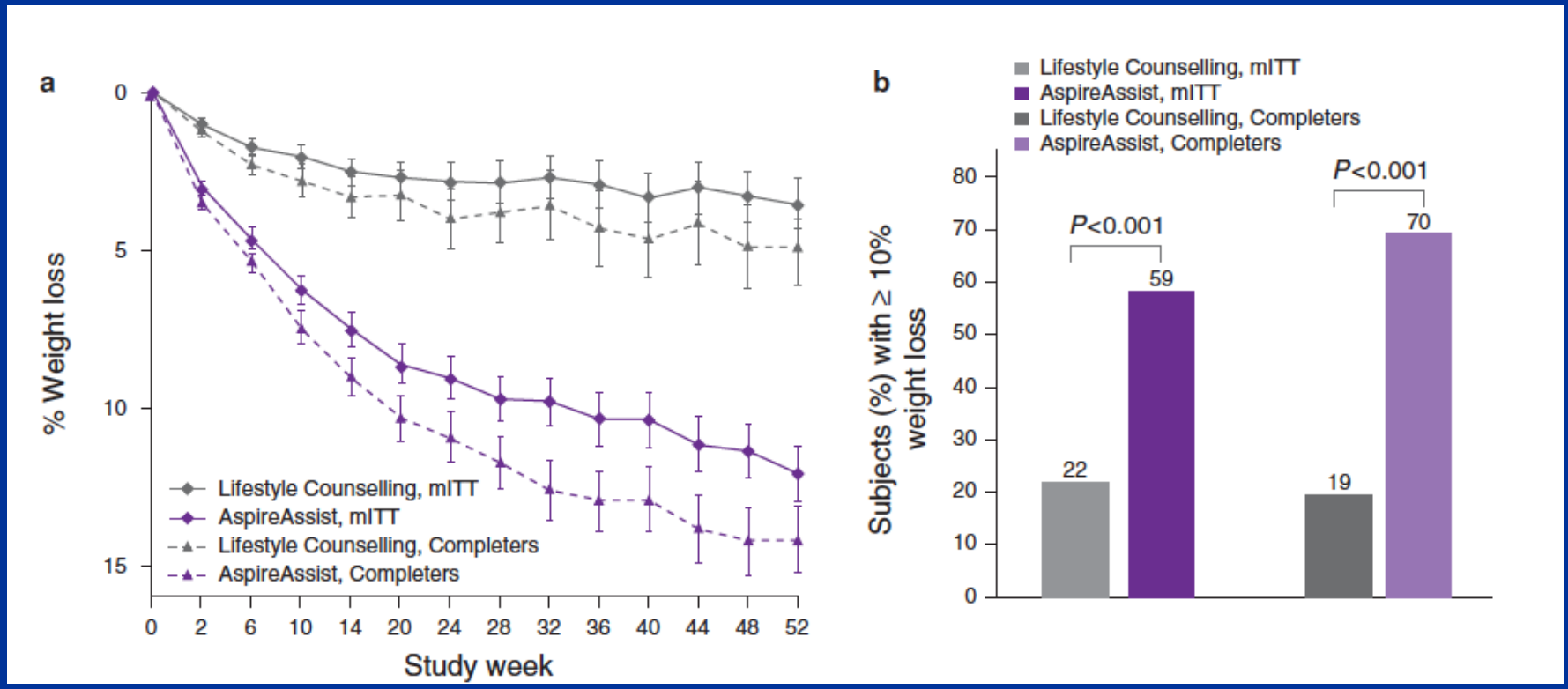


A. A-tube
B. Aspire Assist device

Aspire Bariatrics, King of Prussia, PA

- Large silicone gastrostomy tube (A-tube) placed endoscopically using standard pull PEG technique
- Connected to Aspire Assist device
- Patient siphons off a third of ingested meal
- Works by diversion of calories and change in behavior causing decreased food intake (chewing longer, drinking more water)

Aspire efficacy



Average weight loss 14.2%, with 59% of patients reaching 10% TWL

Thompson CC, Abu Dayyeh BK, Kushner R et al. Percutaneous gastrostomy device for the treatment of class II and class III obesity: results of a randomized controlled trial. Am J Gastroenterol 2017; 112:447-457.

Table 2. **Adverse events occurring in 5% or more of participants and serious adverse events in the AspireAssist group (*N*=111), and time period in which the event occurred (i) <7 days (perioperative) and (ii) >7days (postoperative) of A-tube placement**

Adverse events	No. of participants (%)	No. of participants, perioperative	No. of participants, postoperative
Peristomal granulation tissue	45 (40.5%)	0	45
Abdominal pain within 4 weeks after A-tube placement[a]	42 (37.8%)	41	1
Nausea/vomiting	19 (17.1%)	15	4
Peristomal irritation	19 (17.1%)	2	17
Intermittent abdominal discomfort	18 (16.2%)	16	2
Possible or definite peristomal bacterial infection	15 (13.5%)	13	2
Abdominal pain 4 weeks or more after A-tube placement[a]	9 (8.1%)	0	9
Dyspepsia (acid reflux, heartburn, hiccups, belching)	7 (6.3%)	1	6
Peristomal inflammation	6 (5.4%)	4	2
Serious adverse events			
Severe abdominal pain	1 (0.9%)	1	
Peritonitis	1 (0.9%)	1	
Pre-pyloric ulcer	1 (0.9%)		1
A-tube replacement because of Skin-Port malfunction	1 (0.9%)		1

[a]Defined as abdominal pain not relieved with standard oral analgesic therapy.

Thompson CC, Abu Dayyeh BK, Kushner R et al. Percutaneous gastrostomy device for the treatment of class II and class III obesity: results of a randomized controlled trial. Am J Gastroenterol 2017; 112:447-457.

Why endoscopic therapy?

- More weight loss compared with lifestyle therapy and medications
- Less weight loss than surgery, but fewer complications and lower cost
- Only 1-2% of patients eligible for bariatric surgery undergo an operation
- Endoscopy may help fill this treatment gap
- Rapid advancement of this field continues to produce new approaches

Approach to therapy

- Start with lifestyle modification; important to any regimen
- Triage patients to appropriate therapy (medical, endoscopic, surgical)
- Screen for physical and psychological comorbidities; careful patient selection is important
- Program should couple endoscopic therapy with dietary and behavioral counseling

Conclusions

- Multiple EBTs are currently being used in the US for primary obesity treatment, and several studies have shown benefit with large randomized sham controlled and non-sham controlled designs.
- Multiple EBTs are under review by the FDA or are in the investigational phase for FDA approval.
- EBT should be used in conjunction with at least moderate intensity lifestyle therapy as part of a comprehensive long-term weight management program for maximal benefit.

Thank you!

Washington University in St. Louis